=> d his

(FILE 'HOME' ENTERED AT 14:40:00 ON 13 FEB 2001)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 14:40:11 ON 13 FEB 2001

L1 69669 S P21
L2 465 S HISTOCULTURE
L3 2 S L1 AND L2
L4 39364 S FLUORESCEN?(6A)(PROTEIN OR POLYPEPTIDE)
L5 10 S L4 AND L2
L6 6 DUP REM L5 (4 DUPLICATES REMOVED)
L7 2 DUP REM L3 (0 DUPLICATES REMOVED)

=> d au ti so ab l6

L6 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
AU Saito, N. (1); Zhao, M. (1); Li, L. (1); Baranov, E. (1); Katsuoka, K.; Hoffman, R. (1)
TI High efficiency gene transduction and expression of hair follicles in vivo
by ex-vivo adenovirus treatment of histocultured skin.
SO Journal of Investigative Dermatology, (April, 2000) Vol. 114, No. 4, pp. 827.
Meeting Info.: 61st Annual Meeting of the Society for Investigative Dermatology. Chicago, Illinois, USA May 10-14, 2000
ISSN: 0022-202X.

=> d au ti so ab 1-6 l6

L6 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
AU Saito, N. (1); Zhao, M. (1); Li, L. (1); Baranov, E. (1); Katsuoka, K.; Hoffman, R. (1)
TI High efficiency gene transduction and expression of hair follicles in vivo
by ex-vivo adenovirus treatment of histocultured skin.
SO Journal of Investigative Dermatology, (April, 2000) Vol. 114, No. 4, pp. 827.
Meeting Info.: 61st Annual Meeting of the Society for Investigative Dermatology. Chicago, Illinois, USA May 10-14, 2000
ISSN: 0022-202X.

L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
AU Hoffman, Robert M.
TI Green **fluorescent protein** to visualize cancer progression and metastasis
SO Methods Enzymol. (1999), 302(Green Fluorescent Protein), 20-31
CODEN: MENZAU; ISSN: 0076-6879
AB Chinese hamster ovary cells and the human lung adenocarcinoma cell lines ANIP 973 and H-460 were transfected with the dicistronic expression vector
contg. the humanized green **fluorescent protein** (GFP) cDNA. Stable GFP-expressing clones were selected in 1.5 .mu.M methotrexate in vitro and injected s.c. in nude mice. Stable, high-level

expression of GFP was maintained in the s.c. growing tumors. To utilize GFP expression for metastasis studies, fragments of s.c. growing tumor, which were composed of GFP-expressing cells, were implanted by surgical orthotopic implantation (SOI) in the ovary and lung, resp., of nude mice. Subsequent micrometastases were visualized in systemic organs by GFP fluorescence in the lung, liver, brain, skeleton, and other organs down to the single-cell level. With this fluorescence tool, we detected and visualized for the first time tumor cells at the microscopic level in fresh viable tissue in their normal host organ. The results with the GFP-transfected tumor cells, combined with the use of SOI, demonstrate a fundamental advance in the visualization and study of lung cancer metastasis in process. Lung tissue seeded with GFP-expressing ANIP 973 human lung carcinoma cells was incubated in three-dimensional sponge-gel matrix-supported **histoculture**. Tumor progression was continuously visualized by GFP fluorescence in the same individual cultures over a 52-day period, during which time the tumors spread throughout the histocultured lung. **Histoculture** tumor colonization was selective for the growth of lung cancer cells on lung tissue, as no growth occurred on histocultured mouse liver tissue, as also obsd. in vivo. The ability to support selective organ colonization in **histoculture** and visualize tumor progression by GFP fluorescence allows the in vitro study of tumor progression in situ. (c) 1999 Academic Press.

L6 ANSWER 3 OF 6 MEDLINE
AU Chishima T; Miyagi Y; Li L; Tan Y; Baranov E; Yang M; Shimada H; Moossa A R; Hoffman R M
TI Use of **histoculture** and green **fluorescent protein** to visualize tumor cell host interaction [letter].
SO IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY. ANIMAL, (1997 Nov-Dec) 33 (10) 745-7.
Journal code: BZE. ISSN: 1071-2690.

L6 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
AU Chishima, Takasahi; Miyagi, Yohei; Li, Lingna; Tan, Yuyuing; Baranov, Eugene; Yang, Meng; Shimada, Hiroshi; Moossa, A. R.; Hoffman, Robert M. (1)
TI Use of **histoculture** and green **fluorescent protein** to visualize tumor cell host interaction.
SO In Vitro Cellular & Developmental Biology Animal, (Nov.-Dec., 1997) Vol. 33, No. 10, pp. 745-747.
ISSN: 1071-2690.

L6 ANSWER 5 OF 6 MEDLINE DUPLICATE 2
AU Chishima T; Yang M; Miyagi Y; Li L; Tan Y; Baranov E; Shimada H; Moossa A R; Penman S; Hoffman R M
TI Governing step of metastasis visualized in vitro.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Oct 14) 94 (21) 11573-6.
Journal code: PV3. ISSN: 0027-8424.
AB Metastasis is the ultimate life-threatening stage of cancer. The lack of accurate model systems thwarted studies of the metastatic cell's basic biology. To follow continuously the succeeding stages of metastatic colony growth, we heritably labeled cells from the human lung adenocarcinoma cell line ANIP 973 with green **fluorescent protein** (GFP) by transfection with GFP cDNA. Labeled cells were then injected intravenously into nude mice, where, by 7 days, they formed brilliantly fluorescing metastatic colonies on mouse lung [Chishima, T., Miyagi, Y., Wang, X., Yang, M., Tan, Y., Shimada, H., Moossa, A. R. & Hoffman, R. M. (1997)

Clin. Exp. Metastasis 15, 547-552]. The seeded lung tissue was then excised and incubated in the three-dimensional sponge-gel-matrix-supported **histoculture** that maintained the critical features of progressive in vivo tumor colonization while allowing continuous access for measurement and manipulation. Tumor progression was continuously visualized by GFP fluorescence in the same individual cultures over a 52-day period, during which the tumors spread throughout the lung. **Histoculture** tumor colonization was selective for lung cancer cells to grow on lung tissue, because no growth occurred on histocultured mouse liver tissue, which was also observed in vivo. The ability to support selective organ colonization in **histoculture** and visualize tumor progression by GFP fluorescence allows the in vitro study of the governing processes of metastasis [Kuo, T.-H., Kubota, T., Watanbe, M., Furukawa, T., Teramoto, T., Ishibiki, K., Kitajima, M., Moossa, A. R., Penman, S. & Hoffman, R. M. (1995) Proc. Natl. Acad. Sci. USA 92, 12085-12089]. The results presented here provide significant, new opportunities to understand and to develop treatments that prevent and possibly reverse metastasis.

L6 ANSWER 6 OF 6 SCISEARCH COPYRIGHT 2001 ISI (R)
AU Chishima T; Miyagi Y; Li L N; Tan Y Y; Baranov E; Yang M; Shimada H; Moossa A R; Hoffman R M (Reprint)
TI Use of **histoculture** and green **fluorescent protein** to visualize tumor cell host interaction
SO IN VITRO CELLULAR & DEVELOPMENTAL BIOLOGY-ANIMAL, (NOV-DEC 1997) Vol. 33, No. 10, pp. 745-747.
Publisher: SOC IN VITRO BIOLOGY, 9315 LARGO DR WEST, STE 25, LARGO, MD 20774.
ISSN: 1071-2690.

=> d 1-2 au ti so ab l7

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
IN Zhao, Ming
TI Method and model for restoring hair pigmentation caused by tyrosinase gene and melanin biosynthesis disorder
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
AB A compn. and method for treating disorders related to tyrosinase gene expression and melanin biosynthesis is disclosed. The compn. comprises a tyrosinase encoding nucleotide sequence and an ORF-438 encoding nucleotide sequence derived from Streptomyces, adapted for expression in mammalian cells. Also disclosed is a model system for evaluating agents that affect pigmentation, and a method for treating alopecia by gene therapy by providing a gene encoding a cell cycle inhibitor.

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS
IN Lishko, Valeryi; Li, Lingna
TI Method to deliver compositions conferring resistance to alopecia to hair follicles
SO U.S., 41 pp. Cont.-in-part of U.S. 5,641,508.
CODEN: USXXAM
AB The invention describes a method to deliver a compn. selectively to hair follicles using a liposomal formulation. Proteins which are cell cycle inhibitors are products of the multi-drug resistance gene or the recombinant materials for their prodn. are targeted to hair follicles by encapsulating them in liposomes. Rat skin **histocultures** were

5,914,126

pretreated with liposomes contg. p15 proteins, phosphatidylcholine, cholesterol, and phosphatidylethanolamine, then treated with melphalan and doxorubicin; the pretreatment was found to prevent almost completely the chemotherapy-induced alopecia in the skin **histoculture**.

=> d bib l7

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
AN 2000:291242 CAPLUS
DN 132:330595
TI Method and model for restoring hair pigmentation caused by tyrosinase gene and melanin biosynthesis disorder
IN Zhao, Ming
PA Anticancer, Inc., USA
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000024895	A2	20000504	WO 1999-US25118	19991027
	WO 2000024895	A3	20001130		

W: AE, AU, CA, CR, DM, JP, MA, TZ
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1998-105725 19981027
US 1998-105831 19981027

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(FILE 'HOME' ENTERED AT 14:40:00 ON 13 FEB 2001)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 14:40:11 ON 13 FEB 2001

L1 69669 S P21
L2 465 S HISTOCULTURE
L3 2 S L1 AND L2
L4 39364 S FLUORESCEN?(6A)(PROTEIN OR POLYPEPTIDE)
L5 10 S L4 AND L2
L6 6 DUP REM L5 (4 DUPLICATES REMOVED)
L7 2 DUP REM L3 (0 DUPLICATES REMOVED)
L8 115160 S FOLLICLE
L9 28 S L2 AND L8
L10 28 S L9 AND HAIR
L11 13 DUP REM L10 (15 DUPLICATES REMOVED)

=> d 1-13 au ti so l11

L11 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2001 ACS
IN Zhao, Ming
TI Method and model for restoring **hair** pigmentation caused by tyrosinase gene and melanin biosynthesis disorder
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2

L11 ANSWER 2 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
AU Saito, N. (1); Zhao, M. (1); Li, L. (1); Baranov, E. (1); Katsuoka, K.; Hoffman, R. (1)
TI High efficiency gene transduction and expression of **hair follicles** in vivo by ex-vivo adenovirus treatment of histocultured skin.
SO Journal of Investigative Dermatology, (April, 2000) Vol. 114, No. 4, pp. 827.
Meeting Info.: 61st Annual Meeting of the Society for Investigative Dermatology. Chicago, Illinois, USA May 10-14, 2000
ISSN: 0022-202X.

L11 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
AU Zhao, Ming; Saito, Norimitsu; Li, Lingna; Baranov, Eugene; Kondoh, Hirofumi; Mishima, Yutaka; Sugiyama, Masanori; Katsuoka, Kensei; Hoffman, Robert M.
TI A novel approach to gene therapy of Albino **hair** in **histoculture** with a retroviral Streptomyces tyrosinase gene
SO Pigm. Cell Res. (2000), 13(5), 345-351
CODEN: PCREEA; ISSN: 0893-5785

L11 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2001 ACS
IN Miljkovic, Dusan; Geller, Jack; Olbina, Gordana
TI Use of genistein and related compounds to treat certain sex hormone related conditions
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2

L11 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2001 ACS

IN Lishko, Valeryi; Li, Lingna
TI Method to deliver compositions conferring resistance to alopecia to **hair follicles**
SO U.S., 41 pp. Cont.-in-part of U.S. 5,641,508.
CODEN: USXXAM

L11 ANSWER 6 OF 13 MEDLINE DUPLICATE 2
AU Hoffman R M
TI Topical liposome targeting of dyes, melanins, genes, and proteins selectively to **hair follicles**.
SO JOURNAL OF DRUG TARGETING, (1998) 5 (2) 67-74. Ref: 26
Journal code: B3S. ISSN: 1061-186X.

L11 ANSWER 7 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
AU Li, L.; Baranov, E.; Hoffman, R. M.
TI Novel approaches for chemotherapy alopecia: **Histoculture** skin models, apoptosis and liposome **hair-follicle** targeting of proteins and genes.
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1998) Vol. 39, pp. 62.
Meeting Info.: 89th Annual Meeting of the American Association for Cancer Research New Orleans, Louisiana, USA March 28-April 1, 1998 American Association for Cancer Research
. ISSN: 0197-016X.

L11 ANSWER 8 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
AU Li, Lingna; Baranov, Eugene; Hoffman, Robert M.
TI Chemotherapy-induced Alopecia in vitro.
SO In Vitro Cellular & Developmental Biology Animal, (March, 1998) Vol. 34, No. 3 PART 2, pp. 27A.
Meeting Info.: 1998 Meeting of the Society for In Vitro Biology Las Vegas,
Nevada, USA May 30-June 4, 1998 Society for In Vitro Biology
. ISSN: 1071-2690.

L11 ANSWER 9 OF 13 MEDLINE DUPLICATE 3
AU Li L; Hoffman R M
TI The feasibility of targeted selective gene therapy of the **hair follicle**.
SO NATURE MEDICINE, (1995 Jul) 1 (7) 705-6.
Journal code: CG5. ISSN: 1078-8956.

L11 ANSWER 10 OF 13 MEDLINE DUPLICATE 4
AU Paus R; Krejci-Papa N; Li L; Czarnetzki B M; Hoffman R M
TI Correlation of proteolytic activities of organ cultured intact mouse skin with defined **hair** cycle stages.
SO JOURNAL OF DERMATOLOGICAL SCIENCE, (1994 Jun) 7 (3) 202-9.
Journal code: AY9. ISSN: 0923-1811.

L11 ANSWER 11 OF 13 MEDLINE DUPLICATE 5
AU Li L; Margolis L B; Paus R; Hoffman R M
TI **Hair** shaft elongation, **follicle** growth, and spontaneous regression in long-term, gelatin sponge-supported **histoculture** of human scalp skin.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1992 Sep 15) 89 (18) 8764-8.
Journal code: PV3. ISSN: 0027-8424.

L11 ANSWER 12 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 6
AU Li, Lingna; Slominski, Andrezj; Paus, Ralf; Hoffman, Robert M. (1)
TI Skin **histoculture** assay for studying the **hair** cycle.
SO In Vitro Cellular & Developmental Biology, (1992) Vol. 28A, No. 11-12, pp.
695-698.
ISSN: 0883-8364.

L11 ANSWER 13 OF 13 MEDLINE DUPLICATE 7
AU Li L N; Margolis [redacted]; Hoffman R M
TI Skin toxicity determined in vitro by three-dimensional, native-state **histoculture**.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1991 Mar 1) 88 (5) 1908-12.
Journal code: PV3. ISSN: 0027-8424.

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     (FILE 'HOME' ENTERED AT 11:38:06 ON 13 FEB 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 11:38:50 ON 13 FEB
     2003
L1         23374 S ALOPECIA
L2         85023 S P21
L3             1 S L1(8A)L2

=> d bib ab l3

L3   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
AN   2000:291242  CAPLUS
DN   132:330595
TI   Method and model for restoring hair pigmentation caused by tyrosinase gene
     and melanin biosynthesis disorder
IN   Zhao, Ming
PA   Anticancer, Inc., USA
SO   PCT Int. Appl., 27 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ----------------   ----  --------       ---------------  --------
PI   WO 2000024895      A2    20000504       WO 1999-US25118  19991027
     WO 2000024895      A3    20001130
         W:  AE, AU, CA, CR, DM, JP, MA, TZ
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     EP 1127121         A2    20010829       EP 1999-956693   19991027
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     US 6372489         B1    20020416       US 1999-427700   19991027
PRAI US 1998-105725P    P     19981027
     US 1998-105831P    P     19981027
     WO 1999-US25118    W     19991027
AB   A compn. and method for treating disorders related to tyrosinase gene
     expression and melanin biosynthesis is disclosed.  The compn. comprises a
     tyrosinase encoding nucleotide sequence and an ORF-438 encoding nucleotide
     sequence derived from Streptomyces, adapted for expression in mammalian
     cells.  Also disclosed is a model system for evaluating agents that affect
     pigmentation, and a method for treating alopecia by gene therapy by
     providing a gene encoding a cell cycle inhibitor.


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FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 18:54:36 ON 13 FEB 2001

L1 69669 S P21
L2 11856 S CELL(W)CYCLE(6A)INHIBIT?
L3 1648 S L1 AND L2
L4 24512 S FOLLICLE(5A)CELL
L5 2 S L3 AND L4
L6 2 DUP REM L5 (0 DUPLICATES REMOVED)

=> d bib ab 1-2 16

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
AN 1998:324779 CAPLUS
DN 129:19692
TI Method to deliver compositions conferring resistance to alopecia to hair follicles
IN Lishko, Valeryi; Li, Lingna
PA Anticancer, Inc., USA
SO U.S., 41 pp. Cont.-in-part of U.S. 5,641,508.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5753263	A	19980519	US 1995-486520	19950607
	US 5641508	A	19970624	US 1994-181471	19940113
	CA 2159626	AA	19941013	CA 1994-2159626	19940401
	US 5914126	A	19990622	US 1997-858469	19970520
	US 5965157	A	19991012	US 1997-858970	19970520
PRAI	US 1993-41553		19930402		
	US 1994-181471		19940113		
	US 1992-41553		19920402		
	WO 1994-US3634		19940401		
	US 1995-486520		19950607		

AB The invention describes a method to deliver a compn. selectively to hair follicles using a liposomal formulation. Proteins which are **cell cycle inhibitors** are products of the multi-drug resistance gene or the recombinant materials for their prodn. are targeted to hair follicles by encapsulating them in liposomes. Rat skin histocultures were pretreated with liposomes contg. p15 proteins, phosphatidylcholine, cholesterol, and phosphatidylethanolamine, then treated with melphalan and doxorubicin; the pretreatment was found to prevent almost completely the chemotherapy-induced alopecia in the skin histoculture.

L6 ANSWER 2 OF 2 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1998:517751 SCISEARCH
GA The Genuine Article (R) Number: ZX073
TI Hormone-induced proliferation and differentiation of granulosa cells: A coordinated balance of the cell cycle regulators cyclin D2 and p27(Kip1)

AU Robker R L; Richards J S (Reprint)
CS BAYLOR COLL MED, DEPT CELL BIOL, HOUSTON, TX 77030 (Reprint); BAYLOR COLL MED, DEPT CELL BI[redacted], HOUSTON, TX 77030
CYA USA
SO MOLECULAR ENDOCRINOLOGY, (JUL 1998) Vol. 12, No. 7, pp. 924-940.
Publisher: ENDOCRINE SOC, 4350 EAST WEST HIGHWAY SUITE 500, BETHESDA, MD 20814-4110.
ISSN: 0888-8809.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 80

AB The proliferation and terminal differentiation of granulosa cells are critical for normal follicular growth, ovulation, and luteinization. Therefore, the in situ localization and hormonal regulation of cell cycle activators (cyclin D1, D2, and D3) and **cell cycle inhibitors** (p27(Kip1) and **p21**(Cip1)) were analyzed in ovaries of mice and rats at defined stages of follicular growth and differentiation. Cyclin D2 mRNA was specifically localized to granulosa **cells** of growing **follicles**, while cyclin D1 and cyclin D3 were restricted to theca cells. In hypophysectomized (H) rats, cyclin D2 mRNA and protein were increased in granulosa cells by treatment with estradiol or FSH and were increased maximally by treatment with both hormones. In serum-free cultures of rat granulosa cells, cyclin D2 mRNA was rapidly elevated in response to FSH, forskolin, and estradiol, indicating that estradiol as well as cAMP can act directly and independently to increase cyclin D2 expression. The levels of p27(Kip1) protein were not increased in response to estradiol or FSH. In contrast, when ovulatory doses of human CG (LH) were administered to hormonally primed H rats to stimulate luteinization, cyclin D2 mRNA and protein were rapidly decreased and undetectable within 4 h, specifically in granulosa **cells** of large **follicles**. Also in response to LH, the expression of the **cell cycle inhibitor** p27(Kip1) was induced between 12 and 24 h (**p21**(Cip1) was induced within 4 h) and remained elevated specifically in luteal tissue. A critical role for cyclin D2 in the hormone-dependent phase of follicular growth is illustrated by the ovarian follicles of cyclin D2(-/-) mice, which do not undergo rapid growth in response to hormones, but do express markers of FSH/LH action, cell cycle exit, and terminal differentiation. Collectively, these data indicate that FSH and estradiol regulate granulosa cell proliferation during the development of preovulatory follicles by increasing levels of cyclin D2 relative to p27(Kip1) and that LH terminates follicular growth by down-regulating cyclin D2 concurrent with up-regulation of p27(Kip1) and **p21**(Cip1).